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FILE 'HOME' ENTERED AT 09:29:33 ON 05 SEP 2007

=> file caplus medline

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FILE 'MEDLINE' ENTERED AT 09:29:48 ON 05 SEP 2007

=> s ((endothelin? or et-1 or et1 or et 1 or etar?) and (egf or egfr or epidermal growth factor))/ab
L1 480 ((ENDOTHELIN? OR ET-1 OR ET1 OR ET 1 OR ETAR?) AND (EGF OR EGFR OR EPIDERMAL GROWTH FACTOR))/AB

=> S l1 and cancer/ab
L2 43 L1 AND CANCER/AB

=> D l2 1 ibib abs

L2 ANSWER 1 OF 43 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:748964 CAPLUS
TITLE: Combined targeting of endothelin A receptor and epidermal growth factor receptor in ovarian cancer shows enhanced antitumor activity
AUTHOR(S): Rosano, Laura; Di Castro, Valeriana; Spinella, Francesca; Tortora, Giampaolo; Nicotra, Maria Rita; Natali, Pier Giorgio; Bagnato, Anna
CORPORATE SOURCE: Molecular Pathology and Immunology Laboratories, Regina Elena Cancer Institute, Institute of Molecular Biology and Pathology, National Research Council, Rome, Endocrinology and Molecular Oncology Department, University of Naples, Federico II, Naples, Italy
SOURCE: Cancer Research (2007), 67(13), 6351-6359
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ovarian carcinomas overexpress endothelin A receptors (ETAR) and epidermal growth factor (EGF) receptor (EGFR). In these cells, endothelin-1 (ET-1) triggers mitogenic and invasive signaling pathways that are in part mediated by EGFR transactivation. Combined targeting of ETAR, by the specific ETAR antagonist ZD4054, and of EGFR by the EGFR inhibitor gefitinib (IRESSA), may offer improvements in ovarian carcinoma treatment. In HEY and OVCA 433 ovarian carcinoma cells, ET-1 or EGF induced rapid activation of EGFR, p42/44 mitogen-activated protein kinase (MAPK), and AKT. ZD4054 was able to reduce the ET-1-induced EGFR transactivation. Gefitinib significantly inhibited EGF- and ET-1-induced EGFR phosphorylation, but incompletely reduced the ET-1-induced activation of downstream targets. ZD4054 plus gefitinib resulted in a greater inhibition of EGFR, MAPK, and AKT phosphorylation, indicating the critical role of these interconnected signaling proteins. ZD4054

effectively inhibited cell proliferation, invasiveness, and vascular endothelial growth factor (VEGF) secretion. Concomitantly, ZD4054 enhanced apoptosis and E-cadherin promoter activity and expression. In both cell lines, the drug combination resulted in a significant decrease in cell proliferation (65%), invasion (52%), and VEGF production (50%), accompanied by a 2-fold increase in apoptosis. The coadministration of ZD4054 enhanced the efficacy of gefitinib leading to partial (82%) or complete tumor regression on HEY ovarian carcinoma xenografts. Antitumor effects were paralleled by biochem. and immunohistol. evidence of decreased vascularization, Ki-67, matrix metalloproteinase-2 (MMP-2), VEGF, MAPK and EGFR, and enhanced E-cadherin expression. The cross-signaling between the EGFR/ETAR pathways provides a rationale to combine EGFR inhibitors with ETAR antagonists, identifying new effective therapeutic opportunities for ovarian cancer.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l2 2 ibib abs

L2 ANSWER 2 OF 43 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:748943 CAPLUS

DOCUMENT NUMBER: 147:232062

TITLE: Endothelin receptor type B counteracts tenascin-C-induced endothelin receptor type A-dependent focal adhesion and actin stress fiber disorganization

AUTHOR(S): Lange, Katrin; Kammerer, Martial; Hegi, Monika E.; Grotegut, Stefan; Dittmann, Antje; Huang, Wentao; Fluri, Erika; Yip, George W.; Goette, Martin; Ruiz, Christian; Orend, Gertraud

CORPORATE SOURCE: Center for Biomedicine, Department of Clinical and Biological Sciences, Institute of Pathology, University of Basel, Basel, Switz.

SOURCE: Cancer Research (2007), 67(13), 6163-6173
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Tenascin-C, an extracellular matrix mol. of the tumor-specific microenvironment, counteracts the tumor cell proliferation-suppressing effect of fibronectin by blocking the integrin α5{β}1/syndecan-4 complex. This causes cell rounding and stimulates tumor cell proliferation. Tenascin-C also stimulates endothelin receptor type A (EDNRA) expression. Here, we investigated whether signaling through endothelin receptors affects tenascin-C-induced cell rounding. We observed that endothelin receptor type B (EDNRB) activation inhibited cell rounding by tenascin-C and induced spreading by restoring expression and function of focal adhesion kinase (FAK), paxillin, RhoA, and tropomyosin-1 (TM1) via activation of epidermal growth factor receptor, phospholipase C, c-Jun NH2-terminal kinase, and the phosphatidylinositol 3-kinase pathway. In contrast to EDNRB, signaling through EDNRA induced cell rounding, which correlated with FAK inhibition and TM1 and RhoA protein destabilization in the presence of tenascin-C. This occurred in a mitogen-activated protein kinase/extracellular signal-regulated kinase kinase-dependent manner. Thus, tumorigenesis might be enhanced by tenascin-C involving EDNRA signaling. Inhibition of tenascin-C in combination with blocking both endothelin receptors could present a strategy for sensitization of cancer and endothelial cells toward anoikis.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l2 43 ibib abs

L2 ANSWER 43 OF 43 MEDLINE on STN
ACCESSION NUMBER: 91065733 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2249889
TITLE: Mitogenic peptides in breast cyst fluid: relationship with intracystic electrolyte ratios.
AUTHOR: Lai L C; Ghatei M A; Takahashi K; Patel K V; Schrey M P; Ghilchik M W; Bloom S R; James V H
CORPORATE SOURCE: Department of Chemical Pathology, St. Mary's Hospital Medical School, Imperial College of Science, Technology and Medicine, London, UK.
SOURCE: International journal of cancer. Journal international du cancer, (1990 Dec 15) Vol. 46, No. 6, pp. 1014-6. Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 8 Mar 1991
Last Updated on STN: 3 Mar 2000
Entered Medline: 16 Jan 1991

AB Women with palpable breast cysts which are lined with apocrine epithelium may be at higher risk of developing breast cancer than women with breast cysts which are lined with flattened epithelium, the former group being characterized by intracystic sodium to potassium ratios below 3, while the latter group has intracystic sodium to potassium ratios above 3. In this study the distribution of intracystic concentrations of the mitogenic peptides, epidermal growth factor, endothelin and gastrin-releasing peptide in the 2 groups of breast cysts were compared to see whether differences in concentrations between the 2 cyst groups might provide an explanation for the higher risk of breast cancer observed in women with "apocrine" breast cysts. The concentrations of epidermal growth factor and gastrin-releasing peptide were significantly higher in the low electrolyte ratio group (p less than 0.001). There was no difference in endothelin concentrations between the 2 groups. Negative correlations were found between epidermal growth factor concentrations and Na+/K+ and between gastrin-releasing peptide concentrations and Na+/K+ (p less than 0.001). A positive correlation was found between gastrin-releasing peptide and epidermal growth factor concentrations in breast cyst fluid (p less than 0.001). The significantly higher intracystic concentrations of both epidermal growth factor and gastrin-releasing peptide in the low-electrolyte-ratio group may provide an explanation for the higher risk of breast cancer which has been observed in women with "apocrine" breast cysts.

=> d l2 42 ibib abs

L2 ANSWER 42 OF 43 MEDLINE on STN
ACCESSION NUMBER: 96223664 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8630991
TITLE: Endothelin-1 production and decreased endothelin B receptor expression in advanced prostate cancer.
AUTHOR: Nelson J B; Chan-Tack K; Hedican S P; Magnuson S R; Opgenorth T J; Bova G S; Simons J W
CORPORATE SOURCE: James Buchanan Brady Urological Institute Research Laboratories, Johns Hopkins Hospital, Baltimore, Maryland 21287-2411, USA.
CONTRACT NUMBER: CA-58236 (NCI)

SOURCE: Cancer research, (1996 Feb 15) Vol. 56, No. 4, pp. 663-8.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 15 Jul 1996
Last Updated on STN: 3 Mar 2000
Entered Medline: 3 Jul 1996

AB The potent vasoconstrictor endothelin-1 (ET-1) is at its highest concentration in the normal human ejaculate and is associated with the progression of metastatic prostate cancer. ET-1 protein expression is detected in situ in 14 of 14 primary cancers and 14 of 16 metastatic sites of human prostatic carcinoma. Exogenous ET-1 induces prostate cancer proliferation directly and enhances the mitogenic effects of insulin-like growth factor I, insulin-like growth factor II, platelet-derived growth factor, basic fibroblast growth factor, and epidermal growth factor in serum-free conditions in vitro. The ETA-selective receptor antagonist A-127722 inhibits ET-1-stimulated growth, but the ETB-selective receptor antagonist BQ-788 does not. ET-3, an ETB-selective agonist, also had no effect on prostate cancer growth. No specific ETB-binding sites could be demonstrated in any established human prostate cancer cell line tested, and ETB mRNA, detected by reverse transcription PCR, was reduced. The predominance of ETB binding on human benign prostatic epithelial tissue is not present in metastatic prostate cancer by autoradiography. In human prostate cancer progression to metastases, ET-1 and ETA expression are retained, whereas ETB receptor expression is reduced.

=> D l2 41 ibib abs

L2 ANSWER 41 OF 43 MEDLINE on STN
ACCESSION NUMBER: 97238707 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9102218
TITLE: Activation of mitogenic signaling by endothelin 1 in ovarian carcinoma cells.
AUTHOR: Bagnato A; Tecce R; Di Castro V; Catt K J
CORPORATE SOURCE: Laboratory of Molecular Pathology and Ultrastructure, Regina Elena Cancer Institute, Rome, Italy.
SOURCE: Cancer research, (1997 Apr 1) Vol. 57, No. 7, pp. 1306-11.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 24 Apr 1997
Last Updated on STN: 19 Dec 2002
Entered Medline: 17 Apr 1997

AB Endothelin 1 (ET-1) is produced in ovarian cancer cell lines and has been shown to act through ET(A) receptors as an autocrine growth factor to promote tumor cell proliferation in vitro. In OVCA 433 cells, the efficacy of ET-1 as a stimulus of [3H]thymidine incorporation was equivalent to that of epidermal growth factor. ET-1 also stimulated the rapid expression of c-fos, an action mediated by ET(A) receptors. The mitogenic action of ET-

1 was not mediated by a pertussis toxin-sensitive G protein. An analysis of the effects of inhibition and depletion of protein kinase C (PKC) on mitogenic responses demonstrated that PKC was necessary but not sufficient for maximal stimulation by ET-1. In quiescent OVCA 433 cells, ET-1-induced stimulation of [3H]thymidine incorporation was prevented by two structurally distinct inhibitors of tyrosine kinase, herbimycin A and genistein. These results indicate that both PKC and protein tyrosine kinase participate in ET-1-stimulated mitogenic signaling. ET-1 rapidly stimulated tyrosine phosphorylation of several cellular proteins, among which p125FAK and p42 mitogen-activated protein kinase were identified. The additivity between the potent mitogenic actions of ET-1 and epidermal growth factor is consistent with the independence of their signal transduction pathways in ovarian cancer cells. These findings also indicate that intracellular signaling between the ET(A) receptor and a yet unidentified tyrosine kinase is involved in the mitogenic response to ET-1.

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=> s L2 and lung cancer
L3            0 L2 AND LUNG CANCER

=> s l2 and cancer
L4           43 L2 AND CANCER

=> d D l2 40 ibib abs
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REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):
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